Claims

1. A method for delivering a biologically active substance, said method comprising the steps of:

(a) combining said biologically active substance with a macromer;

(b) forming a mixture of the combination formed in step (a);

(c) polymerizing said mixture to form articles; and

(d) administering said articles, or a portion thereof, to a mammal, wherein step (c) takes place in the absence of a polymerizable monovinyl monomer.

2. A method for delivering a biologically active substance, said method comprising the steps of:

(a) combining said biologically active substance with a macromer;

(b) forming a mixture of the combination formed in step (a);

(c) polymerizing said mixture to form articles; and

(d) administering said articles, or a portion thereof, to a mammal, wherein step (c) takes place in the absence of a water soluble polymerizable monovinyl monomer.

3. A method for delivering a biologically active substance, said method comprising the steps of:

(a) combining said biologically active substance with a macromer;

(b) forming a mixture of the combination formed in step (a);

(c) polymerizing said mixture to form articles; and

(d) administering said articles, or a portion thereof, to a mammal,

wherein step (c) takes place in the absence of a vinyl pyrrolidone monomer.

4. The method of claim 1, wherein the time during which 10% of the releasable active substance is released is greater than 1/10 of t_{50}.

5. The method of claim 1, wherein said article comprises at least 2.5% active substance by weight.

6. The method of claim 1, wherein said article comprises at least 5% active substance by weight.

7. The method of claim 1, wherein said article comprises at least 10% active substance by weight.

8. The method of claim 1, wherein said article comprises at least 25% active substance by weight.

9. The method of claim 1, wherein said article comprises at least 40% active substance by weight.

10. The method of claim 1, wherein said macromer comprises:

(a) a water soluble region forming a central core;

(b) at least two degradable regions attached to said core; and

(c) at least two polymerizable end groups, wherein said polymerizable end groups are attached to said degradable regions.

11. The method of claim 10, wherein said water soluble region comprises a polymer selected from the group consisting of poly(ethylene glycol), poly(ethylene oxide), poly(vinyl alcohol), poly(vinylpyrrolidone), poly(ethyloxazoline), poly(ethylene oxide)-co-poly(propylene oxide) block copolymers, polysaccharides, carbohydrates, proteins, and combinations thereof.

12. The method of claim 10, wherein said degradable region comprises a polymer selected from the group consisting of poly(α-hydroxy acids), poly(lactones), poly(amino acids), poly(anhydrides), poly(orthoesters), poly(orthocarbonates) and poly(phosphoesters).

13. The method of claim 10, wherein said degradable region comprises poly(trimethylene carbonate).

14. The method of claim 10, wherein said degradable region comprises poly(caprolactone).

15. The method of claim 12, wherein said poly(α-hydroxy acid) is selected from the group consisting of poly(glycolic acid), poly(DL-lactic acid) and poly(L-lactic acid).

16. The method of claim 12, wherein said poly(lactone) is selected from the group consisting of poly(ε-caprolactone), poly(δ-valerolactone), and poly(γ-butyrolactone).

17. The method of claim 10, wherein said polymerizable end groups contain a carbon-carbon double bond capable of polymerizing the macromers.

18. The method of claim 10, wherein said core comprises poly(ethylene glycol); said degradable regions comprise a biodegradable poly(α-hydroxy acid); and said end caps comprise an acrylate oligomer or monomer.

19. The method of claim 1, wherein step (d) comprises administering said articles to the lung of said mammal.

20. The method of claim 1, wherein step (d) comprises administering said articles intravenously.

21. The method of claim 1, wherein step (d) comprises administering said articles subcutaneously.

22. The method of claim 1, wherein step (d) comprises administering said articles intramuscularly.

23. The method of claim 1, wherein step (d) comprises administering said articles orally.

24. The method of claim 1, wherein step (d) comprises administering said articles nasally.

25. The method of claim 1, wherein said mammal is a human.

26. The method of claim 1, wherein said biologically active substance is a protein.

27. A composition formed by the method of claim 1.

28. A composition formed by the method of claim 2.

29. A composition formed by the method of claim 3.

30. A method for delivering a biologically active substance, said method comprising the steps of:

(a) combining said biologically active substance with a macromer;

(b) forming a mixture of the combination formed in step (a);

(c) polymerizing said mixture to form articles; and

(d) administering said articles, or a portion thereof, to a mammal, wherein said articles release at least 80% of said biologically active substance at a time 2.5 times greater than t_{50}.

31. A method for delivering a biologically active substance, said method comprising the steps of:

(a) combining said biologically active substance with a macromer;

(b) forming a mixture of the combination formed in step (a);

(c) polymerizing said mixture to form articles; and

(d) administering said articles, or a portion thereof, to a mammal, wherein said articles release a therapeutic dose of said biologically active substance for a period of time at least 2.5 times greater than t_{50}.

32. A composition for delivering a biologically active substance, said composition comprising particles comprising a hydrogel and a biologically active substance, wherein the release kinetics of said particles are independent of particle size, wherein said particles have a mass mean diameter of about 50 nm to about 1 mm.

33. A method for making articles for controlled release of a biologically active substance, said method comprising the steps of:

(a) combining said biologically active substance with a biodegradable, polymerizable macromer, said macromer comprising at least one water soluble region, at least one degradable region which is hydrolyzable under *in vivo* conditions, and polymerizable end groups having the capacity to form additional covalent bonds resulting in macromer polymerizing, wherein said polymerizable end groups are separated by at least one degradable region, in the presence of an initiator;

(b) polymerizing said macromer in the absence of light to form a hydrogel and to incorporate said biologically active substance into said hydrogel; and

(c) forming said hydrogel into articles capable of controlled release of said biologically active substance.

34. The method of claim 33, wherein said initiator is a radical initiator.

35. The method of claim 33, wherein said initiator is an ionic initiator.

36. A method for making a polymerized hydrogel, said method comprising the steps of:

(a) combining a hydrophobic, water insoluble macromer, an initiator, and water;

(b) allowing said macromer to swell;

(c) mixing said macromer to form a homogenous mixture; and

(d) polymerizing said macromer to form a hydrogel.

37. The method of claim 36, wherein said method further comprises adding a biologically active substance to said mixture before step (d).

38. A method for making a polymerized hydrogel, said method comprising the steps of:

(a) combining a hydrophilic macromer and a hydrophobic, water insoluble macromer;

(b) heating and stirring the combination formed in step (a) to form a homogenous mixture;

(c) cooling said mixture to room temperature;

(d) adding water and an initiator to said mixture and allowing said mixture to swell; and

(e) polymerizing said macromer to form a hydrogel.

39. The method of claim 38, wherein said method further comprises adding a biologically active substance to said mixture before step (e).

40. A method for delivering a protein, said method comprising the steps of:

(a) combining said protein with a polymerizable hydrophilic polymer;

(b) forming a mixture of the combination formed in step (a);

(c) polymerizing said mixture to form articles; and

(d) administering said articles, or a portion thereof, to a mammal, wherein said protein remains intact, and wherein at least 70% of said protein is released from said articles.

41. A method for delivering a biologically active substance, said method comprising the steps of:

(a) combining said biologically active substance with a biodegradable, polymerizable macromer in an aqueous solution, in the presence of a free radical initiator;

(b) dispersing said solution to form fine droplets comprising said macromer and said biologically active substance;

(c) polymerizing said macromer in the droplets, thereby forming hydrogel particles having said biologically active substance incorporated therein, wherein said particles are capable of controlled release of the biologically active agent; and

(d) administering said articles, or a portion thereof, to a mammal, wherein step (c) takes place in the absence of a vinyl pyrrolidone monomer.

42. The method of claim 41, wherein said solution is dispersed by spray drying or by a water-in-oil emulsion process.

43. The method of claim 41, wherein at least 80% of said particles have a particle size of smaller than about 5 μm.

44. A composition comprising a biologically active substance enclosed within a biodegradable, polymerizable macromer, said macromer comprising at least one water soluble region, at least one degradable region which is hydrolyzable under *in vivo* conditions, and polymerizable end groups having the capacity to form additional covalent bonds resulting in macromer polymerization, wherein said polymerizable end groups are separated by at least one degradable region, wherein said composition contains at least 5% by weight of said biologically active substance.

45. The composition of claim 44, wherein said composition contains at least 10% by weight of said biologically active substance.

46. The composition of claim 44, wherein said composition contains at least 20% by weight of said biologically active substance.

47. An insoluble macromer comprising at least one water soluble region, at least one degradable region which is hydrolyzable under *in vivo* conditions, and polymerizable end groups having the capacity to form additional covalent bonds resulting in macromer polymerization, wherein said polymerizable

end groups are separated by at least one degradable region.

48. The macromer of claim 47, wherein said degradable region comprises a blend of at least two different polymers.

49. The macromer of claim 47, wherein said degradable region comprises a copolymer of at least two different monomers.

50. The macromer is claim 47, wherein said water soluble region comprises at least 2 arms.

51. The macromer of claim 47, wherein said water soluble region consists essentially of poly(ethylene glycol) having a molecular weight of about 400 to 8000 daltons.

52. A composition for the sustained delivery of a protein, wherein said composition comprises an insoluble macromer comprising at least one water soluble region, at least one degradable region which is hydrolyzable under *in vivo* conditions, and polymerizable end groups having the capacity to form additional covalent bonds resulting in macromer polymerization, wherein said polymerizable end groups are separated by at least one degradable region.

53. A macromer comprising at least one water soluble region, at least one degradable region which is hydrolyzable under *in vivo* conditions, and polymerizable end groups having the capacity to form additional covalent bonds resulting in macromer polymerization, wherein said polymerizable end groups are

separated by at least one degradable region, wherein said degradable region consists essentially of poly(trimethylene carbonate).

54. A composition for the subcutaneous administration of LHRH, wherein said composition comprises a core of poly(ethylene glycol) having a molecular weight of about 1000 daltons, and a degradable region consisting of poly(caprolactone) , wherein said composition is capable of delivering a therapeutic dose of LHRH for more than 30 days.

55. A composition comprising glucacon like peptide-1 and a macromer, said macromer comprising at least one water soluble region, at least one degradable region which is hydrolyzable under *in vivo* conditions, and polymerizable end groups having the capacity to form additional covalent bonds resulting in macromer polymerization, wherein said polymerizable end groups are separated by at least one degradable region.

56. A hydrogel composition for the sustained release of a biologically active substance, wherein said composition comprises particles having a tap density of less than 0.4 g/cm^3, wherein at least 50% of said particles have a mass mean diameter of less than about 5 μm, and wherein said composition is formulated for pulmonary administraton.

57. A composition for the sustained release of a biologically active substance, wherein said composition comprises particles having a tap density of more than 0.4 g/cm^3.

58. The composition of claim 57, wherein said composition is formulated for pulmonary delivery.